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(21) International Application Number: PCT/EP97/03411 (22) International Filing Date: 1 July 1997 (01.07.97) (30) Priority Data: MI96A001354 2 July 1996 (02.07.96) IT MI96A002275 31 October 1996 (31.10.96) IT (71) Applicant (for all designated States except US): SYLVIE LIMITED [---]; Wickham's Cay, Road Town, Tortola (VG). (72) Inventors; and (75) Inventors/Applicants (for US only): FERRARIO, Gianluigi [IT/-]; Wickham's Cay, Road Town, Tortola (VG). BAR-TORELLI, Luisa [IT/TT]; Via A. Fogazzaro, 20, I-20135 Milano (IT). (74) Agent: BIANCHETTI, Giuseppe; Studio Consulenza Brevetuale, Via Rossini, 8, I-20122 Milano (IT).			(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
(54) Title: PHARMACEUTICAL FORMULATIONS CONTAINING COLOSTRUM AND THEIR USE			
(57) Abstract  Pharmaceutical formulations containing animal colostrum for the treatment of intestine inflammatory diseases and anorectal disturbances, and the use of colostrum for the treatment of intestine inflammatory diseases and anorectal disturbances.			

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## PHARMACEUTICAL FORMULATIONS CONTAINING COLOSTRUM AND THEIR USE

The present invention relates to pharmaceutical formulations containing animal colostrum for the treatment of intestine inflammatory diseases and anorectal disturbances, and the use of colostrum for the treatment of intestine inflammatory diseases and anorectal disturbances.

The etiology of chronic inflammatory diseases of the intestine, such as Crohn' disease, ulcerative colitis and segmentary ileitis, is still unknown: a number of immunological, bacterial, dietetic and psychosomatic factors have been considered, but up to now no definite hypothesis have been proved. The treatment of said diseases involves, in addition to dietetic measures, the use of corticosteroids, immunosuppressors, antibiotics, antibacterials and psychoactive drugs. Since such diseases have a chronic course, or relapses and remissions alternate, the need for a treatment alternative to the long-term ones with the above mentioned drugs is evident. Finally, in the most serious cases, which do not respond to any treatment, surgery is taken into consideration.

Anorectal disturbances such as hemorrhoids, anorectal fistulas and anal fissures can be the outcome of vascular problems, of inflammatory conditions of the intestinal tract, or they can be of a traumatic or congenital origin. All of said conditions are characterized by a remarkable worsening of the symptoms

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(pain, bleeding) following defecation, therefore the treatment consists in the use of rectum lubricants and of agents making stools softer (natural or semi-synthetic polysaccharides and cellulose derivatives such as bran, psyllium and methylcellulose) thanks to an increased absorption of liquids in the intestinal tract. However, such an approach is not always sufficient to resolve the condition, and it is often necessary to resort to surgery, which often involves a long, rather painful post-surgery course. Therefore a valid alternative to surgery is highly desirable.

The present invention aims at overcoming the above cited problems, by the use of pharmaceutical formulations containing equine, bovine or anyhow animal, but preferably equine, colostrum, for the treatment of intestine inflammatory diseases and anorectal disturbances.

The present invention further relates to the use of equine, bovine or anyhow animal, but preferably equine, colostrum, for the treatment of intestine inflammatory diseases and anorectal disturbances.

It has surprisingly been found that colostrum, administered to patients suffering from intestine inflammatory diseases and anorectal disturbances, exerts a remarkable antiinflammatory and epithelizing action on the involved tract of intestine, thus improving the general conditions of the treated patient, particularly causing the disappearance of bleeding, abdomen cramps and diarrhoea crisis typical of these conditions. Moreover, colostrum acts favourably inducing effectively and physiologically the evacuation, without causing any

side-effects.

In fact, clinical trials on 20 patients, showed a favourable response of 17 patients to the treatment with colostrum, attaining in very short times a remarkable improvement in the symptoms.

The pharmaceutical formulations of invention contain powder or liquid colostrum in amounts of 500 mg to 5 g per unitary dose.

More particularly, the formulations of the invention comprise gastro-resistant formulations such as tablets containing powdered, freeze-dried or sprayzed colostrum or pearls containing liquid colostrum, as well as rectal formulations such as suppositories containing powdered, freeze-dried or sprayzed colostrum or enemas containing liquid colostrum.

The formulations of invention are prepared according to the conventional pharmaceutical techniques for the preparation of gastro-resistant and rectal formulations.

The enteric coating is used to protect colostrum against the gastric acid environment, such a coating can consist of copolymerized methacrylic acid/methacrylic acid methyl esters, such as those known under the names Eudragit<sup>R</sup> (commercialized by Rohm Pharma), polymers such as cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, water-based polymer dispersions, such as Eudragit<sup>R</sup> (by Rohm Pharma), Aquateric<sup>R</sup> (FMC Corp.). The enteric coating can optionally contain plasticizers such as triacetin, cetanol, citric and phthalic acids esters.

The formulations of the invention can optionally

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contain other active ingredients known to have a beneficial effect on the condition to treat.

According to a further aspect of the invention, the formulations can contain colostrum mixed with milk.

5       The following examples further illustrate the invention.

**Example 1**

One enteric-coated tablet contains:

	Powder colostrum	110 mg
10	Hydroxypropyl methylcellulose phthalate	6 mg
	Cetyl alcohol	0.5 mg

The enteric coating solution is applied on the colostrum core by fluidized bed coating.

**Example 2**

15       One enteric-coated tablet contains:

	Powder colostrum	64 mg
	Powder milk	45 mg
	Hydroxypropyl methylcellulose phthalate	32 mg
	Cetyl alcohol	5 mg

20       The enteric coating solution is applied on the colostrum core by fluidized bed coating.

**Example 3**

One suppository contains:

	Powder colostrum	250 mg
25	Saturated polyglycosylated glycerides	150 mg
	Solid semi-synthetic glycerides	2600 mg

**Example 4**

Enema

	Powder colostrum	300 mg
30	Saturated polyglycosylated glycerides	150 mg
	Saturated triglycerides	1550 mg

CLAIMS

1. Pharmaceutical formulations containing colostrum for the treatment of intestine inflammatory diseases and anorectal disturbances.
2. Pharmaceutical formulations according to claim 1, wherein the colostrum is equine, bovine or anyhow animal, but preferably equine, colostrum.
3. Formulations according to claims 1 and 2, in the form of gastro-resistant formulations or rectal formulations.
4. Gastro-resistant formulations according to claim 3, in the form of tablets containing powdered, freeze-dried or sprayzed colostrum or pearls containing liquid colostrum.
5. Rectal formulations according to claim 3, in the form of suppositories containing powdered, freeze-dried or sprayzed colostrum or enemas containing liquid colostrum.
6. Formulations according to the above claims, containing 500 mg to 5 g of powder or liquid colostrum per unitary dose.
7. Formulations according to claims 3 and 4, wherein the powder colostrum is freeze-dried or sprayzed.
8. Formulations according to the above claims, further containing powder milk.
9. The use of colostrum for the preparation of a medicament for the treatment of intestine inflammatory diseases and anorectal disturbances.

# INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/EP 97/03411

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K35/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 527 283 A (SOCIETE DES PRODUITS NESTLE S.A.) 17 February 1993 see page 3, line 10 - line 17; claims ---	1-9
A	WO 93 25227 A (KABI PHARMACIA AB) 23 December 1993 see page 1, paragraph 1; claims see page 4, line 14 - line 15 ---	1-9
P, A	WO 96 34614 A (GROPEP PTY. LTD.) 7 November 1996 see page 6, line 6 - line 10; claims -----	1-9

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No  
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